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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,911	02/08/2005	Scott D. Kuduk	21216YP	9456
210	7590	12/06/2005	EXAMINER	
MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			AULAKH, CHARANJIT	
			ART UNIT	PAPER NUMBER
			1625	
DATE MAILED: 12/06/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/523,911	Applicant(s) KUDUK ET AL.	
	Examiner Charanjit S. Aulakh	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 and 4-26 is/are allowed.
- 6) ☒ Claim(s) 2,3 and 27-32 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1 Page</u> . | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

1. Claims 1-32 are pending in the application.

Specification

2. This application does not contain an abstract of the disclosure as required by 37

CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 27-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858. F. 2d 731, 8 USPQ 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight factors such as quantity of experimentation

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necessary, the amount of direction or guidance provided, the state of the prior art, presence of working examples and the breadth of claims.

The specification teaches on page 15 that the instant compounds are antagonists of bradykinin B1 receptors and mentions assays on page 21 for assessing B1 receptor antagonist activity. The specification also teaches on page 1 that B1 receptors are not expressed in normal tissues and are only induced following inflammation, tissue damage or bacterial infection. However, there is no teaching in the specification or prior art reference mentioned in the specification regarding induction or upregulation of bradykinin B1 receptors in any specific painful or inflammatory disease condition. There is no mention of any animal model for even a single disease condition where bradykinin B1 receptor antagonists have been shown to be effective. There are no working examples present to assess the efficacy of bradykinin B1 receptor antagonists in an animal model of any type of pain or inflammation or any disease condition. Furthermore, there is no teaching either in the specification or prior art that upregulation (increased number of receptors) of bradykinin B1 receptors is the only known mechanism responsible for mediating all kinds of pain and inflammation or pain and inflammation associated with all disease conditions mentioned in instant claims 28, 30 and 32. There is no teaching in the specification or presence of working examples to show how the instant compounds having inhibitory activity at only bradykinin B1 receptors will have utility in treating/preventing pain or inflammation or any disease condition which is not mediated by bradykinin B1 receptors. The instant compounds of formula I encompasses hundreds of thousands of compounds based on variables R1-R7, Het. and m and

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therefore, in absence of such teachings, guidance and presence of working examples, it would require undue experimentation to assess the effectiveness of the instant compounds in animal models of every known painful or inflammatory disease condition and hence their utility in treating every type of known or yet unknown pain or inflammation or pain/ inflammation associated with all disease conditions mentioned in instant claims 28, 30 and 32.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2, 3, 27, 29, 30 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2, the value of variable R5 is further defined. However, it is not clear whether 1,2,5-thiadiazolyl, isoxazolyl, isothiazolyl or pyrimidinyl is defined directly as a value of variable R5 or as substituents of C1-6 alkyl group?

In claim 3, line 2, the term ---group--- is indefinite since its meaning is not clear.

In claims 27, 29, 30 and 32, the term --- prevention--- is indefinite since the degree of prevention (20%, 40%, 60%, 80% or 100%) is not defined and furthermore, it is not clear how this prevention is being assessed following in vivo administration of instant compounds?

Allowable Subject Matter

7. The following is a statement of reasons for the indication of allowable subject matter:

The instant compounds are allowable over the prior art since they are neither disclosed

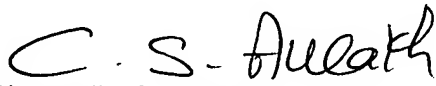
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nor obvious over the prior art. In the prior art, Wood (U.S. Patent no. 6,919,343, cited on applicants form 1449) discloses compounds of formula I (see col. 2, lines 1-65) which are closely related to instant compounds. However, the compounds of Wood differ in structure from the instant compounds in having a phenyl ring instead of a pyridyl or pyrimidyl ring attached to the phenyl group.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Charanjit S. Aulakh
Primary Examiner
Art Unit 1625